Buprenorphine Transdermal System (TDS) [BUTRANS] C-III
Criteria for Use
June, 2016

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information. For further information, see the VA National PBM-MAP-VPE supporting Drug Monograph for these criteria at www.pbm.va.gov or http://vaww.pbm.va.gov.

Transitioning Veteran *Buprenorphine TDS is on the DoD VHA Transitional Continuity of Care Drug List; if the criterion is met, the remainder of the criteria for use is not applicable.*

☐ Veteran is transitioning care from the Department of Defense to VHA. A VA prescriber, after assessing and consulting with the Veteran, has determined that continuation of buprenorphine TDS is safe and clinically appropriate.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive buprenorphine TDS (BTDS):*

☐ Intended use is for treatment of acute pain or postoperative pain
☐ Intended use is as an as-needed (prn) analgesic
☐ Intended use is treatment of opioid use disorder
☐ Patient has significant respiratory depression, conditions predisposing to significant respiratory depression including acute or severe bronchial asthma, or known/suspected paralytic ileus
☐ Patient has hypersensitivity to buprenorphine
☐ Patient has long QT Syndrome (or family history of same), or is taking a Class IA or Class III antiarrhythmic medication

Inclusion Criteria *The following criteria must be fulfilled for provision of buprenorphine TDS (BTDS):*

Indication is management of moderate to severe chronic pain requiring a continuous, around-the-clock opioid analgesic for an extended period of time

AND

- There is documentation of inadequate analgesic response despite adequate trials of at least three (3) immediate-release opioid analgesic agents (e.g. tramadol, codeine/acetaminophen, hydrocodone/acetaminophen, oxycodone/acetaminophen) **AND** there is documentation of intolerance, contraindication, or risk factor for potentially serious adverse effects to lower-potency oral formulary extended-release opioid analgesic agents.†

OR

- Patient has documented difficulty swallowing, poor or unpredictable gastrointestinal absorption (e.g., short bowel; nausea, vomiting).

Practice Standards for Provision of Chronic Opioid Therapy – General principles, defined by CDC and VA/DoD Clinical Practice Guidelines for prescribing of opioids for chronic pain, should be utilized to guide management of long-term opioid therapy. Practitioners should obtain informed consent from each patient after explaining the risks, benefits, and obligatory terms of long term treatment with opioids. All federal and state guidelines on prescribing and dispensing opioids should be strictly followed. There should be an initial and periodic checking of the respective State(s) Prescription Drug Monitoring System (if available), consideration of provision of naloxone rescue, and exercise of other strategies to mitigate risk of chronic opioid therapy.

† "Lower potency oral formulary extended-release opioid analgesics" includes morphine SA and oxycodone SA (but not oxymorphone SA); methadone is a long-acting opioid and not extended-release

Dosage and Administration

- BTDS should be prescribed only by providers who are knowledgeable in the use of potent opioids for the management of chronic pain.
- BTDS is available for prescribing in doses of 5, 7.5, 10, 15, and 20 mcg/hour.
- **A dose of one 20 mcg/hour BTDS should not be exceeded because of the risk of QTc prolongation.**
- **Opioid naïve patients:** BTDS should be initiated with a 5 mcg/hour patch; patients should be monitored closely for respiratory depression over the initial 24-72 hours
- **Opioid-experienced patients:**
  General Considerations
  - All other around-the-clock opioid drugs should be discontinued when BTDS therapy is initiated.
  - There is a potential for buprenorphine to precipitate withdrawal in patients who are already on opioids.
  - Actual *conversion* doses are not necessarily *equianalgesic* doses, and equianalgesic dose ratios may differ by the order of switching opioids and the reasons for switching (e.g., for adverse reactions or inadequate analgesia).
  - The *conversion* doses recommended in the US product information are conservative; thus, supplemental short-acting opioid therapy will likely be necessary to achieve adequate analgesia when converting from another opioid to

BTDS. The analgesic effect of the short-acting opioid may be less predictable in the context of concurrent buprenorphine treatment. Also, opioid abstinence symptoms may occur if the substitute and supplemental opioid doses are insufficient to prevent opioid withdrawal in patients who are physically opioid-dependent.
    - In clinical practice, BTDS 10 mcg/hour is approximately equivalent to an oral morphine equivalent daily dose (MEDD) of 18-28 mg, and BTDS 20 mcg/hour is approximately equivalent to a MEDD of 36-55 mg.

  Conversion from other opioids to BTDS:
    - *Prior Total Daily Dose of Opioid Less than 30 mg of Oral MEDD*: BTDS 5 mcg/hour should be initiated at the next dosing interval.
    - *Prior Total Daily Dose of Opioid Between 30 mg to 80 mg of Oral MEDD*: The patient's current around-the-clock opioids should be tapered (over a period of up to 7 days) to no more than an oral MEDD of 30 mg before beginning treatment with BTDS. Then BTDS 10 mcg/hour should be initiated at the next dosing interval. Patients may use short-acting analgesics as needed until analgesic efficacy with BTDS 10 mcg/h (or, with titration, 20 mcg/hour) is attained.
    - *Prior Total Daily Dose of Opioid Greater than 80 mg of Oral MEDD*: The maximum dose of BTDS 20 mcg/hour may not provide adequate analgesia for patients requiring greater than 80 mg/day oral morphine equivalents. An alternate analgesic should be considered.
    - *Conversion from Methadone to BTDS:* Close monitoring is of particular importance. The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure.
- The dose of BTDS does not need to be adjusted in patients with mild or moderate hepatic impairment, renal impairment or in the elderly.
- When the patient no longer requires therapy with BTDS, a gradual down-titration of dose should be performed every 7 days to prevent signs and symptoms of withdrawal. Consider introduction of an appropriate immediate-release opioid medication.

Administration Instructions and Disposal

- Patients should apply BTDS to the upper outer arm, upper chest, upper back or the side of the chest on either side of the body (total of 8 application sites). Patients should be instructed to wait a minimum of 21 days before reapplying BTDS to the same skin site. Reapplication of BTDS to the same site before 21 days may result in increased drug absorption.
- If BTDS falls off during the 7-day dosing interval, the patient should dispose of the transdermal system properly and place a new BTDS patch on at a different skin site.
- Patients may dispose of used or unused BTDS in the trash by sealing the patches in the Patch-Disposal Unit packaged with BTDS.
- Alternatively, patients can dispose of used patches by folding the adhesive side of the patch to itself, then flushing the patch down the toilet immediately.

Safety

- Concomitant use of BTDS with CNS depressants, including benzodiazepines, may cause profound sedation, respiratory depression, and death. If coadministration is required, consider dose reduction of one or both drugs because of additive pharmacological effects.
- Monitor elderly, cachectic, debilitated patients, and those with chronic pulmonary disease closely because of increased risk of respiratory depression.
- Avoid use of BTDS in patients with Long QT Syndrome, family history of Long QT Syndrome, or those taking Class IA or Class III antiarrhythmic medications.
- BTDS has hypotensive effects warranting monitoring of blood pressure during dose initiation and titration.
- Avoid use of BTDS in patients with impaired consciousness or coma, head injury or increased intracranial pressure.
- Initiating or discontinuing CYP3A4 inducers may result in alteration of buprenorphine plasma concentrations; for additional information, *see the VA National PBM-MAP-VPE supporting Drug Monograph.*
- BTDS is Pregnancy Category C; women of childbearing potential should be provided contraceptive counseling on potential risk vs. benefit of taking BTDS if they were to become pregnant. BTDS should only be used during pregnancy if the benefit to the mother outweighs the potential risk to the fetus.
- Use of opioids during pregnancy can prolong labor and result in respiratory depression, physical dependence and withdrawal syndrome in the neonate.
- Buprenorphine is excreted in breast milk and opioid withdrawal symptoms can occur in infants when mothers discontinue BTDS therapy. Discontinue nursing or discontinue the drug, taking into account the importance of the medication to the mother.
- Application of external heat sources increased the maximum plasma concentration (Cmax) of buprenorphine by 26% to 55% relative to application without heat. Patients should be advised to avoid hot baths, sunbathing, using hot tubs, saunas, heating pads, electric blankets, heated waterbeds, or tanning lamps because of the risk of fatal overdose. Fever (internal heat) was not shown to alter the pharmacokinetics of buprenorphine from BTDS application.

Issues for Consideration

- There are several proposed advantages of buprenorphine over full mu-agonists including antihyperalgesic effects, a respiratory depression ceiling effect (in the absence of other CNS depressants), lower risk of hormonal effects, lack of immunosuppression, and only moderate withdrawal symptoms. Lack of tolerance has also been proposed.
- In contrast to fentanyl TDS, BTDS has a lower abuse liability and is approved for initiation of opioid therapy and use in opioid-naïve patients.
- Due to the high receptor affinity of buprenorphine, in the event of an overdose, greater than usual doses of naloxone and a

longer time to onset of mu-receptor antagonist effects (e.g., 1–3 hours) may be required to reverse respiratory depression.

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